ANDA 75-388 February 15, 2000

Applied Analytical Industries, Inc.
Attention: Lois Q. Semmens
U.S. Agent for: PharmEx Products, Inc.
2320 Scientific Park Drive
Wilmington, NC 28405

Dear Madam:

This is in reference to your abbreviated new drug application dated May 26, 1998, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (Act), for Buspirone Hydrochloride Tablets USP, 5 mg, 10 mg, and 15 mg.

Reference is also made to your amendments dated January 26, July 16, August 9, and December 17, 1999; and February 8, 2000.

We have completed the review of this abbreviated application and have concluded that based upon the information you have presented to date, the drug is safe and effective for use as recommended in the submitted labeling. Therefore, the application is **tentatively approved**. This determination is based upon information available to the Agency at this time, (i.e., information in your application and the status of current good manufacturing practices (CGMPs) of the facilities used in the manufacture and testing of the drug product), and is subject to change on the basis of new information that may come to our attention. This letter does not address notice issues related to the 180-day exclusivity provisions under section 505(j)(5)(B)(iv) of the Act.

The listed drug product (RLD) referenced in your application, BuSpar Tablets of Bristol Myers Squibb Co. Pharmaceutical Research Institute, is subject to periods of patent protection which expire on May 22, 2000, (U.S. patent 4,182,763, the '763 patent) and May 14, 2008, (U.S. patent 5,015,646, the '646 patent). Your application

contains a Paragraph IV Certification to the '646 patent under Section 505(j)(2)(A)(vii)(IV) of the Act stating that the patent is invalid or unenforceable or that it will not be infringed by your commercial manufacture, use, or sale of this drug product. Section 505(j)(5)(B)(iii) of the Act provides that approval shall be made effective immediately unless an action is brought for infringement of the patent which is the subject of the certification before the expiration of forty-five days from the date the notice provided under paragraph (2)(B)(i) is received. You have notified the agency that PharmEx Products, Inc. (PharmEx) has complied with the requirements of Section 505(j)(2)(B) of the Act and that no action for infringement of the '646 patent was brought against PharmEx within the statutory forty-five day period. In addition, your application contains a Paragraph III Certification to the '763 patent under Section 505(j)(2)(A)(vii)(III) of the Act. Therefore, final approval of your application may not be made effective pursuant to 21 U.S.C. 355(j)(5)(B)(ii) of the Act until the ‘763 patent has expired, i.e., currently May 22, 2000.

Because the agency is granting a tentative approval for this application, please submit an amendment to this application at least 60 days (but not more than 90 days) prior to the date you believe your application will be eligible for final approval. This amendment should identify changes, if any, in the conditions under which the product was tentatively approved and should include updated information such as final-printed labeling (including appropriate changes made to the approved labeling of the RLD), as well as updated chemistry, manufacturing, and controls data as appropriate. Furthermore, the regulations state (21 CFR 314.95) that an applicant must address each listed patent and provide a patent certification for each reference listed drug. Your amendment providing for the 15 mg strength does not provide complete information with regard to patent certification and notification. We note your contention as stated in your February 8, 2000 submission that a separate notification to the patent holder regarding the 15 mg strength is unnecessary. Since the agency regards each strength of a reference listed drug (RLD) as a separate RLD, you should notify the RLD holder and provide appropriate of documentation of receipt of the notice as well as the RLD holder’s response as part of this amendment. Without such documentation, the agency will not

approve the 15 mg strength. This amendment should be clearly designated as a MINOR AMENDMENT in your cover letter. In addition to, or instead of this amendment, the Agency may request at any time prior to the date of final approval of this application that you submit an amendment containing the information described above. Failure to submit either or, if requested, both amendments may result in rescission of the tentative approval status of your application, or may result in a delay in the issuance of the final approval letter.

Any significant change in the conditions outlined in this abbreviated application, as well as changes in the status of the manufacturing and testing facilities' compliance with current good manufacturing practices (CGMPs) are subject to agency review before final approval of the application will be made.

This drug product may not be marketed without final agency approval under Section 505 of the Act. The introduction or delivery for introduction of this drug product into interstate commerce before the final approval date is prohibited under Section 501 of the Act. Also, until the agency issues the final approval letter, this drug product will not be listed in the "Approved Drug Products with Therapeutic Equivalence Evaluations" list (the "Orange book"), published by the agency.

Should you believe that there are grounds for issuing the final approval letter prior to the expiration of the '763 patent on
May 22, 2000, you should amend your application accordingly.

Prior to submitting an amendment, please contact Ms. Ruby Yu, Pharm.D, Project Manager, at (301)827-5848, for further instructions.

Sincerely yours,

Douglas L. Sporn
Director

Office of Generic Drugs
Center for Drug Evaluation and Research